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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/789,355 | 02/27/2004 | George Kukolj | 13/083-3-D2 | 9062 |

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| EXAMINER | |
|---|---|
| LI, BAO Q | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1648 | |

DATE MAILED: 12/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/789,355 | KUKOLJ ET AL. | |
| | Examiner | Art Unit | |
| | Bao Qun Li | 1648 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *21 November 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) *2* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 3-6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *02/27/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Election/Restrictions*

1. Applicant's election of group I, claims 1 and 3-6 in the scope of mutation at amino acid residue 2040 from G to C or G to R in the reply filed on 11/21/2005 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. The requirement is still deemed proper and is therefore made FINAL.

*3.* Claims 1 and 3-6 in the scope of G(2042)C and G(2042)R are considered.

### *Sequence requirements*

4. This application contains sequence disclosures on pages 4-5,7, 11 and 15 that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

5. Full compliance with the sequence rules is required in response to this Office Action. A complete response to this office action should include both compliance with the sequence rules and a response to the Office Action set forth below. Failure to fully comply with **both** these requirements in the time period set forth in this office action will be held non-responsive.

### *Claim Rejections - 35 USC § 101*

3. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The invention of claim 1 is directed to non-statutory subject matter. There is no recitation of isolation or synthesis in front of the claimed HCV polynucleotide. Therefore, the claimed product read on naturally occurring HCV genome, which are considered to be non-statutory and non-patentable subject matter within the scope of 35 U.S.C. 101. See Official Gazett, 1077 O.G. April 21, 1987. It is recommended that the claim incorporate the claim language, " isolated or molecular cloned" to overcome this rejection.

***Claim Rejections - 35 USC § 112***

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1 and 3-6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6. Claim 1 is vague in that the structural characteristic of claimed HCV self-replication polynucleotide is not defined, i.e. where does the numeric number of the first amino acid residue start. Please amend the claim with a precise sequence identification number, which enable the examiner to search and examine the claimed invention properly. Applicants can claim some additional mutation in a HCV genome; however, Office needs to know which basic non-mutated HCV genome sequence is. This affects the dependent claims 3-6.

***Claim Rejections - 35 USC § 112***

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1 and 3-6 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while enabling for isolating a self-replication HCV genome encoded by the

polynucleotide sequence selected from group consisting of SEQ ID NO: 1, 2, 4, 5, 6, 7 24 and 25, in which the amino acid residue at the position 2042 is mutated from G to C or G to R, does not reasonably provide enablement for having any or all HCV self-replicating polynucleotide having such mutation at the position 2042. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

9. Nature of invention and scope of claims: The present invention is directed to several isolated HCV self replication clones from the HCV transformed host cell Huh-7 cell clones, and some of them comprises a particular mutation at the position o 2042 with substitutive mutation from G to C or G to R that enables the HCV self-replicating clone can be replicate well without cytotoxicity to the host cell. The polynucleotide sequence is selected from group consisting of SEQ ID NO: 2, 4, 5, 6, 7. 24 or 25 having such mutation. However, the scope of claimed invention is drawn to any HCV genome comprising such mutation.

10. State of art and unpredictability: Hepatitis C virus (HCV) is a quasisspecies of RNA virus. Currently at least six major genotypes (1-6) and a number of subtypes. Moreover, each HCV isolate exhibits different mutation. The efficiencies of the HCV replicons change greatly according to the frequently uncounted random mutation(s) of HCV genome as evidenced by Wimmer et al. (US Patent 6, 689,559B2, see columns 1-3). However, the efficiency for a HCV 1b replicone change greatly if the HCV 5A contains some random of mutations that result in successfully isolation of several transfected Huh-7 cell clones as taught by Blight et al. (Science 2000,Vol. 290, pp. 1972-1974). Therefore, it is unpredictably for isolating any HCV polynucleotide having such mutation at position 2042..

11. Working example and guidance of the specification: The specification only teaches a few isolated HCV transformed Huh-7 cell clones that are able to replicate well in the transfected host cell without significantly inhibiting the host cell's viability, wherein such HCV has a particular sequence identified by the sequence identified number from 2, 4, 5, 6, 7 24 and 25. Applicants do not provide adequate teaching and guiding about any or all HCV replicon as claim 1 drafted that is able to transfect a host cell line without significantly inhibiting the host cell's viability.

12. Hence, considering large quantity of experimentation needed, the unpredictability of the field, the state of the art, and breadth of the claims, it is concluded that undue experimentation would be required to enable the full scope of the rejected claims.

***Conclusion***

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao Qun Li whose telephone number is 571-272-0904. The examiner can normally be reached on 7:00 am to 3:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

BAOQUN LI, MD
PATENT EXAMINER

BQ Li

Bao Qun Li
12/22/2005